



## **Hyundai Hope on Wheels Hyundai Scholar Research**

**Dr. Duncan Stearns**  
Rainbow Babies & Children's Hospital – Cleveland, OH

### **The Role of Oncogene MYC in Medulloblastoma**

Medulloblastoma is the most common malignant brain tumor in childhood. While many children can be cured with current therapies, over 1/3 still die from their cancer. Even for those who survive their disease, most suffer lifelong disability of variable degree. With continued research into novel therapies that cause less damage to the developing brain and nervous system, there is hope that more children will survive this disease with fewer long-term side effects.

Previous work has shown that there are numerous signs that make medulloblastoma tumors more likely to recur, less likely to respond to current treatments. Tumor anaplasia is characterized by several specific microscopic features and is a sign of "high risk" medulloblastoma. High levels of the oncogene, MYC, have been associated both with "high risk" tumors and tumor anaplasia. MYC is a gene important for many normal cell functions, but is found to be abnormally expressed in many cancers. Little is known about what it does in medulloblastoma.

In a model system using tumor cells forced to express high levels of MYC, cells grow more quickly and form larger tumors in animals. These changes mimic many features of anaplasia. In other cancers, MYC changes the levels of many thousands of other genes to make tumors more dangerous. We are using these experimental, high-MYC cells to try to learn the mechanisms underlying "high risk" disease by examining the changes in gene expression patterns. In this way, we may identify additional markers for use in treatment decisions as well as, hopefully, designing new treatments for patients with the worst tumors.

Several groups of genes have already been identified and are undergoing additional study. For example, MYC seems to drastically change the make-up of the scaffolding that surrounds the tumor cells, the so-called extracellular matrix (ECM). Traditionally, research has focused on the cancer cells themselves and the pathways that are important for tumor growth and spread. In medulloblastoma, there is very little known about the role of the ECM. The make-up of the ECM varies greatly between different organs in the body and is often

altered in malignancy. In many other cancers, this matrix plays important roles in cell survival and invasion. The matrix is also very important in normal brain development. Preliminary results indicate that the matrix in many medulloblastoma tumors is very different from that of normal brain and that the tumor cells themselves actively contribute to the ECM. This raises the possibility that targeting the matrix in medulloblastoma may damage tumor cells, but not normal nervous tissue, the goal of developing less neurotoxic therapies.

The additional funding provided by the Hyundai Scholar award will allow an expansion of the study of MYC and medulloblastoma. The first round of experiments has identified almost 2000 genes that may be changed by MYC. Many of these are likely to be not important in all tumors, so a careful analysis is required to screen out the candidates that will not be helpful in patients. To do this, additional medulloblastoma tumors will be tested. These will be derived from experimental systems and, when available, from patient tumor samples. This will help identify the most common, important genes that then can be tested for possible treatment strategies. The Hyundai Scholar award will be targeted for personnel and material costs and will be instrumental in advancing this project.